

Preferably, a protein expression vector (described in the specification of a patent application entitled "Protein expression vector and its use" and filed by the same applicant on the same day) is used. This expression vector is constructed by using pCRII-TOPO vector described in the Examples hereinafter, or a commercially available expression vector, for example pSecTag2A vector or pSecTag2B vector (Invitrogen) and integrating a secretory signal nucleotide sequence suitable for expression of the protein of the present invention, in the 3' downstream side thereof, a Tag nucleotide sequence, a cleavable nucleotide sequence and a cloning site, into which a nucleotide sequence encoding a target protein can be inserted, in this order. More specifically, it is preferred to use trypsin signal as the secretory signal, a nucleotide sequence encoding polyhistidine as the Tag nucleotide sequence, and a nucleotide sequence encoding an amino acid sequence which is susceptible to enzyme-specific cleavage, i.e., a nucleotide sequence encoding the amino acid sequence of Asp-Asp-Asp-Asp-Lys (SEQ ID NO:40) (said amino acid sequence is recognized by enterokinase, and the recombinant fusion protein is cleaved at the C-terminus part thereof) as the cleavable nucleotide sequence.--

Please replace the paragraph beginning at the bottom of page 59, line 19, with the following rewritten paragraph:

--Amplification was carried out by using the primers having the sequences represented by SEQ ID NOS: 11 and 12 so that the peptide of Leu-Val-His-Gly (SEQ ID NO:41) was present

at the C-terminus of the part from trypsin signal to the enterokinase recognition site of pSecTrypHis/neurosin. This was inserted between NheI and HindIII sites of pSecTag2A to construct the plasmid pTrypSig.--

IN THE CLAIMS

Please add new claims 42-53 as follows:

--42(New). A protein selected from the group consisting of:

(a) a protein having the amino acid sequence composed of 229 amino acids represented by the 1st to 229th amino acids of SEQ ID NO:2;

(b) a protein having an amino acid sequence derived from the amino acid sequence represented by the 1st to 229th amino acids of SEQ ID NO:2 by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the 1st to 229th amino acids of SEQ ID NO:2;

(c) a protein having the amino acid sequence composed of 229 amino acids represented by the 1st to 229th amino acids of SEQ ID NO:4;

(d) a protein having an amino acid sequence derived from the amino acid sequence represented by the 1st to 229th amino acids of SEQ ID NO:4 by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the 1st to 229th amino acids of SEQ ID NO:4;

(e) a protein having the amino acid sequence composed of 282 amino acids represented by the -53rd to 229th amino acids of SEQ ID NO:2;

(f) a protein having an amino acid sequence derived from the amino acid sequence represented by the -53rd to 229th amino acids of SEQ ID NO:2 by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the -53rd to 229th amino acids of SEQ ID NO:2;

(g) a protein having the amino acid sequence composed of 250 amino acids represented by the -21st to 229th amino acids of SEQ ID NO:2;

(h) a protein having an amino acid sequence derived from the amino acid sequence represented by the -21st to 229th amino acids of SEQ ID NO:2 by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the -21st to 229th amino acids of SEQ ID NO:2;

(i) a protein having the amino acid sequence composed of 249 amino acids represented by the -20th to 229th amino acids of SEQ ID NO:4;

(j) a protein having an amino acid sequence derived from the amino acid sequence represented by the -20th to 229th amino acids of SEQ ID NO:4 by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the -20th to 229th amino acids of SEQ ID NO:4;

(k) a protein having the amino acid sequence

composed of 276 amino acids represented by the -47th to 229th amino acids of SEQ ID NO:4;

(l) a protein having an amino acid sequence derived from the amino acid sequence represented by the -47th to 229th amino acids of SEQ ID NO:4 by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the -47th to 229th amino acids of SEQ ID NO:4;

(m) a protein having the amino acid sequence composed of 254 amino acids represented by the 1st to 254th amino acids of SEQ ID NO:6;

(n) a protein having an amino acid sequence derived from the amino acid sequence represented by the 1st to 254th amino acids of SEQ ID NO:6 by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the 1st to 254th amino acids of SEQ ID NO:6;

(o) a protein having the amino acid sequence composed of 275 amino acids represented by the -21st to 254th amino acids of SEQ ID NO:6; and

(p) a protein having an amino acid sequence derived from the amino acid sequence represented by the -21st to 254th amino acids of SEQ ID NO:6 by deletion, substitution or addition of one to several amino acids and having the same property as that of the protein having the amino acid sequence represented by the -21st to 254th amino acids of SEQ ID NO:6; and

(q) a modified derivative or fragment of these

proteins (a) to (p).

43(New). A nucleotide sequence selected from the group consisting of:

(aa) a nucleotide sequence of nucleotides 272 to 958 of SEQ ID NO:1;

(bb) a nucleotide sequence encoding the amino acid sequence of residues 1 to 229 of SEQ ID NO:2;

(cc) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (aa) or (bb) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues 1 to 229 of SEQ ID NO:2;

(dd) a nucleotide sequence of nucleotides 244 to 930 of SEQ ID NO:3;

(ee) a nucleotide sequence encoding the amino acid sequence of residues 1 to 229 of SEQ ID NO:4;

(ff) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (dd) or (ee) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues 1 to 229 of SEQ ID NO:4;

(gg) a nucleotide sequence of nucleotides 113 to 958 of SEQ ID NO:1;

(hh) a nucleotide sequence encoding the amino acid sequence of residues -53 to 229 of SEQ ID NO:2;

(ii) a nucleotide sequence hybridizable with a

nucleotide sequence which is complementary to the above nucleotide sequence (gg) or (hh) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues -53 to 229 amino acids of SEQ ID NO:2;

(jj) a nucleotide sequence of nucleotides 209 to 958 of SEQ ID NO:1;

(kk) a nucleotide sequence encoding the amino acid sequence of residues -21 to 229 of SEQ ID NO:2;

(ll) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (jj) or (kk) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues -21 to 229 of SEQ ID NO:2;

(mm) a nucleotide sequence of nucleotides 184 to 930 of SEQ ID NO:3;

(nn) a nucleotide sequence encoding the amino acid sequence of residues -20 to 229 of SEQ ID NO:4;

(oo) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (mm) or (nn) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues -20 to 229 of SEQ ID NO:4;

(pp) a nucleotide sequence of nucleotides 103 to 930 of SEQ ID NO:3;

(qq) a nucleotide sequence encoding the amino acid

sequence of residues -47 to 229 of SEQ ID NO:4;

(rr) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (pp) or (qq) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues -47 to 229 of SEQ ID NO:4.

(ss) a nucleotide sequence of nucleotides 114 to 875 of SEQ ID NO:5;

(tt) a nucleotide sequence encoding the amino acid sequence of residues 1 to 254 of SEQ ID NO:6;

(uu) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (ss) or (tt) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues 1 to 254 of SEQ ID NO:6;

(vv) a nucleotide sequence of nucleotides 51 to 875 of SEQ ID NO:5;

(ww) a nucleotide sequence encoding the amino acid sequence of residues -21 to 254 of SEQ ID NO:6;

(xx) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (vv) or (ww) under stringent conditions and encoding a protein having the same property as that of the protein having the amino acid sequence of residues -21 to 254 of SEQ ID NO:6;

(yy) a nucleotide sequence of SEQ ID NO:1;

(zz) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (yy) under stringent conditions and encoding a protein having the same property as that of the protein encoded by the nucleotide sequence of SEQ ID NO:1;

(aaa) a nucleotide sequence of SEQ ID NO:3;

(bbb) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (aaa) under stringent conditions and encoding a protein having the same property as that of the protein encoded by the nucleotide sequence of SEQ ID NO:3;

(ccc) a nucleotide sequence of SEQ ID NO:5;

(ddd) a nucleotide sequence hybridizable with a nucleotide sequence which is complementary to the above nucleotide sequence (ccc) under stringent conditions and encoding a protein having the same property as that of the protein encoded by the nucleotide sequence of SEQ ID NO:5; and

(eee) a fragment of these nucleotide sequences (aa) to (ddd).

44(New). A process for producing a protein which comprises culturing cells transformed with the nucleotide sequence (dd), (ee), (ff), (mm), (nn), (oo), (pp), (qq), (rr), (aaa) or (bbb) of claim 43, and collecting mBSSP6 produced.

45(New). The process according to claim 44, wherein the cells are *E. coli* cells, animal cells or insect cells.

46(New). A process for producing a protein which comprises culturing cells transformed with the nucleotide sequence (ss), (tt), (uu), (vv), (ww), (xx), (ccc) or (ddd) of

claim 43 and collecting mutant hBSSP6 produced.

47(New). The process according to claim 46, wherein the cells are *E. coli* cells, animal cells or insect cells.

48(New). The method according to claim 34, wherein the specimen is a body fluid.

49(New). The method according to claim 35, wherein the specimen is a body fluid.

50(New). A method for screening for an inhibitor of serine protease comprising comparing the enzyme activity of the protein according to claim 42 upon bringing the protein into contact with a candidate compound with the enzyme activity of the protein without contact with the candidate compound.

51(New). A pharmaceutical composition comprising the protein according to claim 42.

52(New). A method for detecting a diagnostic marker for diseases in tissues comprising the protein according to claim 42 which comprises using the antibody against the protein according to claim 42.

53(New). The method according to claim 52, wherein the marker is used for diagnosis of a cancer.--

Please replace claims 20-22, 30, 32-35 and 37 with new amended claims 20-22, 30, 32-35 and 37 as follows:

20(Amended). A vector comprising the nucleotide sequence according to claim 43.

21(Amended). Transformed cells having the nucleotide sequence according to claim 43 in an expressible

state.

22(Amended). A process for producing a protein which comprises culturing cells transformed with the nucleotide sequence (aa), (bb), (cc), (gg), (hh), (ii), (jj), (kk), (ll), (yy) or (zz) of claim 43, and collecting hBSSP6 produced.

30(Amended). An antibody against the protein according to claim 42 or a fragment thereof.

32(Amended). A process for producing a monoclonal antibody against the protein according to claim 42 or a fragment thereof which comprises administering the protein according to claim 42 or a fragment thereof to a warm-blooded animal other than a human being, selecting the animal whose antibody titer is recognized, collecting its spleen or lymph node, fusing the antibody producing cells contained therein with myeloma cells to prepare a monoclonal antibody producing hybridoma.

33(Amended). A method for determining the protein according to claim 42 or a fragment thereof in a specimen which is based on immunological binding of an antibody against the protein or a fragment thereof to the protein or a fragment thereof.

34(Amended). A method for determining BSSP6 or a fragment thereof in a specimen which comprises reacting a monoclonal antibody or a polyclonal antibody against the protein (a), (b), (e), (f), (g), (h), (m), (n), (o) or (p) of claim 42 or a modified derivative thereof or a fragment thereof and a labeled antibody with BSSP6 or a fragment

thereof in the specimen to detect a sandwich complex produced.

35(Amended). A method for determining BSSP6 or a fragment thereof in a specimen which comprises reacting a monoclonal antibody or a polyclonal antibody against the protein (a), (b), (e), (f), (g), (h), (m), (n), (o) or (p) of claim 42 or a modified derivative thereof or a fragment thereof with labeled BSSP6 and BSSP6 or a fragment thereof in the specimen competitively to detect an amount of BSSP6 or a fragment thereof in the specimen based on an amount of the labeled BSSP6 reacted with the antibody.

37(Amended). A diagnostic marker for diseases in tissues comprising the protein according to claim 42, or a fragment thereof.

IN THE SEQUENCE LISTING

Please substitute the paper copy Sequence Listing attached hereto for the Sequence Listing originally filed.

REMARKS

The amendments to the claims are made to place the application in better condition for examination.

Applicants have added into the present specification a substitute paper copy Sequence Listing section according to 37 C.F.R. §1.821(c). Furthermore, attached hereto is a 3 1/2" disk containing the "Sequence Listing" in computer readable form in accordance with 37 C.F.R. §1.821(e).